THE

SCIENTIFIC PROCEEDINGS

OF THE

ROYAL DUBLIN SOCIETY

VOL. 24 (N.S.).

COMMONWEALTH MYCOLOGICAL INSTITUTE
8 SEP. 1948

[SEPARATE ISSUE.]

No. 28. SEPTEMBER 6, 1948.

THE CHEMICAL CONSTITUENTS OF LICHENS FOUND IN IRELAND.

BUELLIA CANESCENS. PART 3.

THE CONSTITUTION OF DIPLOICIN.

BY

(The late) THOMAS J. NOLAN, JOSEPH ALGAR, EUGENE P. MCCANN, WILLIAM A. MANAHAN AND NIALL NOLAN.

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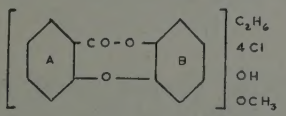
University College, Dublin.

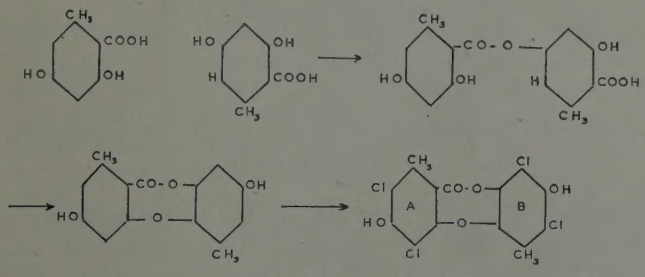
[Read MARCH 23. Published Seperately, SEPTEMBER 6, 1948.]

IN Part 2 of this investigation it was shown by Spillane, Keane, and Nolan (Sci. Proc. R.D.S. 1936, **21**, p. 333) that the lichen *Buellia Canescens* contains, amongst other substances, the compound diploicin, to which they gave the formula $C_{16}H_{10}O_5Cl_4$. It was also shown by these workers that diploicin is a depsidone and that to it could be attributed the structure :—



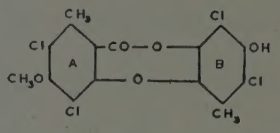
(I)

It was surmised that the C_2H_6 consisted of two methyl groups, rather than an ethyl group and a hydrogen atom, and that diploicin resulted from the condensation of two molecules of orsellinic acid, with subsequent elimination of one carboxyl group and simultaneous oxidation and chlorination. This would result in the compound II the monomethyl ether of which would be diploicin.



(II)

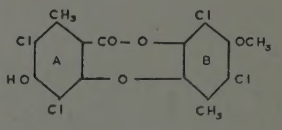
By analogy with known lichen substances it was regarded as most likely that the hydroxyl group in ring A had been methylated to form diploicin, which would accordingly have the structure III.



(III)

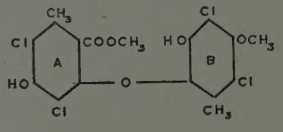
It should be noted that evidence so far given in proof of this configuration is limited to establishing the formula I, and that the complete formula III is based on analogy. A Kuhn-Roth determination of C-methyl has since been carried out and indicates the presence of two C-methyls, thus confirming the earlier surmise.

In the present communication, degradation experiments on diploicin are described which appear to prove that the structure of diploicin is correctly represented by the formula IV.



which places the methyl ether grouping in ring B and not in ring A, as was considered likely in the previously cited communication.

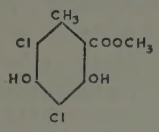
The orientation of the groups in ring A has been established in the following way. On treatment of diploicin with methyl alcoholic potash, the lactone bridge is opened to form the ester V (Spillane, Keane, and Nolan, *loc. cit.*).



(V)

2.4.3′.5′–*tetrachlor*—3.2′–*dihydroxy*—6–*carbomethoxy*—4′–*methoxy*—5.6′–*dimethyl diphenyl ether.*

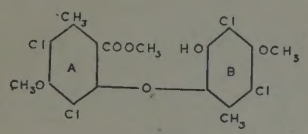
The breakdown of the ester V by fission of the oxygen bridge was accomplished in the following way. The ester was subjected to super-chlorination, followed by reduction and hydrolysis. This resulted in the production of 4..6–dichlor-orsellinic acid methyl ester VI.



(VI)

a substance which has been synthesised by Nolan and Murphy (Sci. Proc. R.D.S. 1940, **22,** p. 317). Control experiments in the case of gangaleoidin (Davidson, Keane, and Nolan, Sci. Proc. R.D.S. 1943, **23,** p. 143) had shown that super-chlorination does not result in demethylation, and consequently it was probable that the methoxyl group of diploicin, by inference, was in ring B. Definite proof of the occurrence of the free hydroxyl group in ring A was forthcoming from the following procedure.

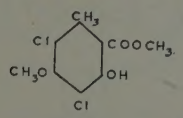
Diploicin was methylated, and the lactone bridge then opened to form the ester VII (Spillane, Keane, and Nolan *loc. cit.*).



(VII)

2.4.3′.5′–*tetrachlor*—2′–*hydroxy*—6–*carbomethoxy*—3.4′–*dimethoxy*—5.6′–*dimethyl diphenyl–ether.*

The ester VII was super-chlorinated, and on reduction and hydrolysis gave the mono-methyl ether of 4.6–dichlor–orsellinic acid methyl ester VIII.

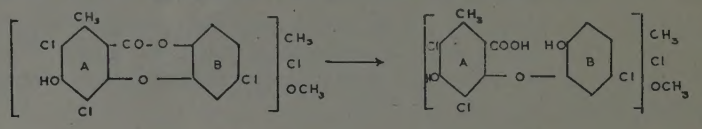


(VIII)

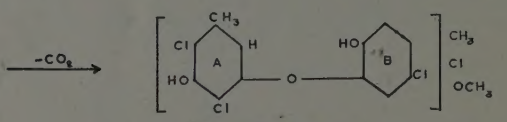
thus proving that the original methoxyl group in diploicin is in ring B and not in ring A. In the work so far described, no product was isolated which gave a clue to the orientation of the groups in ring B. It seemed likely that the most profitable method to isolate this half of the diploicin molecule, or a derivative thereof, would be to demethylate diploicin, and examine the nature of the product obtained, by submitting the resultant material to alkaline hydrolysis. Before doing so, the ester VII was examined for its colour reaction with 2.6–dichlorquinone–chlorimide in a sodium borate buffer solution. This reaction has been employed by Todd and Hems (J.C.S., 1940, p. 1208) as a test for a hydrogen atom para to a hydroxyl group in a benzene ring. Davidson, Keane, and Nolan (*loc. cit.*) have shown that it applies not only to hydrogen para to hydroxyl but also to certain negative substituents

para to hydroxyl. Thus, para chlorphenol gives an intense blue, para hydroxy benzoic acid a deep blue, but para hydroxy benzoic ester gives no definite colour reaction. Now diploicin gives no definite colour reaction, but when the lactone bridge is opened to form the ester VII, thus setting free a hydroxyl group in ring B, a deep blue colour is obtained on testing. This colour reaction is therefore strong presumptive evidence for the presence of a chlorine atom in ring B in a position para to the oxygen atom of the lactone bridge (see IX).

When diploicin is subjected to alkaline hydrolysis and the resulting product is subjected to further hydrolysis or heated above its melting point, a series of compounds is obtained which may be explained in the following way :—



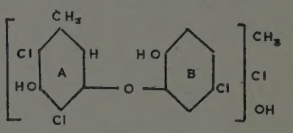
(IX)



(X)

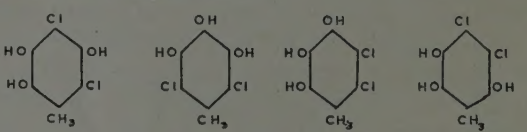
that is to say, a substituted di-tolyl ether is produced.

On the other hand, when diploicin is heated with hydrobromic acid in acetic acid solution, the lactone bridge is opened and the product is simultaneously decarboxylated and demethylated, giving rise to the substituted di-tolyl ether XI.



(XI)

The methylated di-tolyl ether X is resistant to the action of alcoholic potash, but the demethylated product XI is readily attacked, and fission of the oxygen bridge takes place. On the assumption that the process is hydrolytic, ring B in XI could give rise to the following products :—

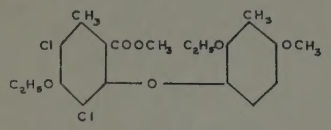


(XII) (XIII) (XIV) (XV)

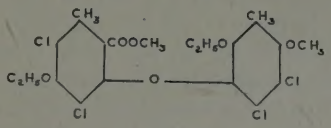
while ring A should give 4·6-dichlor-orcinol.

The structure XV, as a possible product, was excluded in the following manner by Nolan (see article by T. J. Nolan on Lichen Substances, Thorpe's Dictionary of Chemistry, 1946, p. 299).

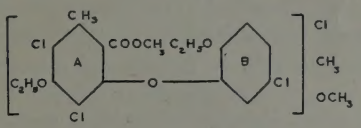
From gangaleoidin was prepared the substance



which on chlorination gave



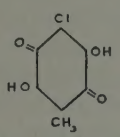
melting point 76°–77°C. which was not identical with the compound



melting point 94°–95°C., prepared from diploicin by treatment with methyl alcoholic potash, followed by treatment with diazo-ethane.

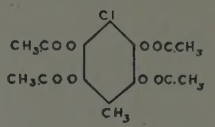
It follows therefore, that the possible products of hydrolysis arising from ring B are XII, XIII or XIV, which, in their turn, might by a process of oxidation give rise to a toluquinone containing chlorine and hydroxyl groups.

When the di-tolyl ether XI was subjected to the action of methyl alcoholic potash, in the presence of oxygen, the only pure product isolated was a mono-chlor di-hydroxy toluquinone $C_7H_5O_4Cl$. On the assumption that this toluquinone originated from 2·4-dichlor trihydroxy toluene XII it could have the formula



(XVI)

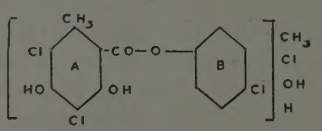
and, for reasons stated below, it seems certain that the substance is correctly represented by this structure. This toluquinone crystallises in very characteristic garnet-coloured hexagonal plates which give a violet coloration with a dilute solution of sodium carbonate. On reduction with sulphur dioxide and subsequent acetylation it gave the tetracetate of 4–chlor–2·3·5·6–tetrahydroxy toluene XVII, which melts at 219°C.



(XVII)

It was essential, therefore, to determine whether the toluquinone obtained from the di-tolyl ether XI, originated from 2·4–dichlor trihydroxy toluene XII, 2·6–dichlor trihydroxy toluene XIII, or 2·3–dichlor trihydroxy toluene XIV. The latter three compounds were prepared by us, and their synthesis is described in the experimental part. On examining their behaviour with methyl alcoholic potash, it was found impossible to isolate a toluquinone from the products of the reaction with 2·6–dichlor trihydroxy toluene or with 2·3–dichlor trihydroxy toluene. On the other hand, when 2·4–dichlor trihydroxy toluene was treated with methyl alcoholic potash, we were able to isolate a mono-chlor dihydroxy toluquinone, which crystallised in garnet coloured hexagonal plates and gave a violet coloration with dilute sodium carbonate. On reduction with sulphur dioxide and subsequent acetylation it gave the tetracetate of 4–chlor–2·3·5·6–tetrahydroxy toluene. M.P. 219°C.

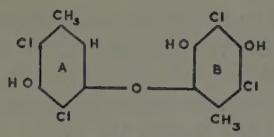
Further confirmation of the structure of diploicin was obtained in the following manner. When diploicin, in benzene solution, was heated with anhydrous aluminium chloride, a product was obtained which appeared to have the structure XVIII.



(XVIII)

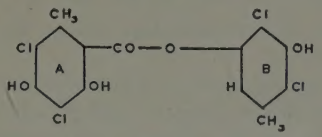
This substance formed a trimethyl ether and a triacetate, and on treatment with methyl alcoholic potash gave two products. One of these was the methyl ester of 4·6–dichlor orsellinic acid VI, and originated from ring A. The second product, derived from ring B, crystallised in garnet-coloured hexagons, identical with XVI, as on reduction and acetylation it gave the tetracetate of a mono-chlor tetrahydroxy toluene, M.P. 219°C., the mixed melting point of which with XVII was unchanged. These facts appear definitely to exclude the possibility of the toluquinone having its origin in ring A, since 4·6–dichlor orsellinic ester remains practically unaltered when treated with methyl alcoholic potash under similar conditions (see Nolan and Murphy, Sc. Proc. R.D.S. 1940, **33**, p. 317).

It is clear, therefore, that the same toluquinone was obtained by the action of methyl alcoholic potash on the di-tolyl ether XI, on the compound XVIII, and on 2·4–dichlor trihydroxy toluene XII. The groupings present in the latter substance must therefore be present in the di-tolyl ether XI, which may therefore be formulated



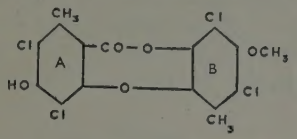
2·4·3′·5′–tetrachlor—3·2′·4′–trihydroxy—5·6′–dimethyl diphenyl ether

and the structure of XVIII may be represented by



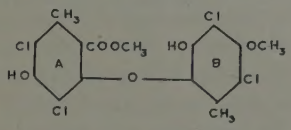
(*2·4–dichlor—3–hydroxy—5–methyl*) *phenyl ester of* 4·6*–dichlor–orsellinic acid.*

Consequently the formula for diploicin must be



EXPERIMENTAL PART.

Action of Chlorine followed by reduction and hydrolysis on the Compound V.



(M)

To a solution of the above compound (0·5 g.) in chloroform (60 c.c.) was added 13·3 c.c. of a solution of chlorine in carbon tetrachloride containing 0·04 g. chlorine per c.c. After standing for 24 hours in a stoppered flask, the excess chlorine was removed by blowing dry air through the solution, and the solvents removed by evaporation. The residue was a brownish gum. The latter was reduced in acetic acid solution (25 c.c.) with stannous chloride (1 g.) in twenty per cent. hydrochloric acid (30 c.c.). The latter solution was added in portions at a temperature of about 40°C. A precipitate was formed immediately. After standing overnight, water (50 c.c.) was added and the supernatant liquid decanted from the solid, which was then washed with a little five per cent. hydrochloric acid, followed by water, and air dried. The solid was refluxed gently with ten per cent. methyl alcoholic potash (25 c.c.) in an atmosphere of hydrogen for one hour. The solution was then diluted with water, acidified, and extracted with ether. The ether solution was successively extracted with three per cent. solutions of (*a*) sodium bicarbonate and (*b*) sodium carbonate.

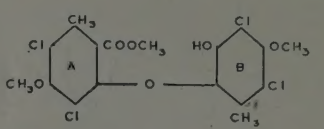
(*a*) The sodium bicarbonate extract was acidified and the precipitated material subjected to steam distillation, giving a white crystalline material in the distillate. On crystallisation of this material from aqueous methyl alcohol, colourless crystals were obtained M.P. 115°C., identical with the 4·6–dichlor orsellinic acid methyl ester (VI) prepared by Nolan and Murphy (*loc. cit.*).

Found :— C40·2, H3·8, Cl 26·0.

$C_9H_8O_4Cl_2$, H_2O requires :— C40·14, H3·71, Cl 26·4.

(*b*) Acidification of the sodium carbonate extract mentioned above, gave the original substance V, unaltered.

Action of Chlorine followed by reduction and hydrolysis on the Compound VII.



(VII)

The above compound (0·55 g.) was dissolved in chloroform (30 c.c.) and to it was added a solution of chlorine in carbon tetrachloride (6·5 c.c.) containing 0·085 g. of chlorine per c.c. The mixture was allowed to stand five days in a stoppered flask, excess chlorine was removed in a stream of dry air, and the solvents removed by evaporation. The residual oil was dissolved in acetic acid (40 c.c.) and reduced with stannous chloride (1·2 g.) dissolved in twenty per cent. hydrochloric acid (40 c.c.). After standing overnight, the mixture was diluted with water and extracted with chloroform. After washing with water, the chloroform solution was evaporated, leaving an oil. The latter was refluxed with ten per cent. methyl alcoholic potash (30 c.c.) for one hour, in a hydrogen atmosphere. The mixture thus obtained was cooled, diluted with water, acidified with dilute sulphuric acid, and extracted with ether. The ether solution was successively extracted with (*a*), three per cent. sodium bicarbonate and (*b*), one per cent. sodium hydroxide.

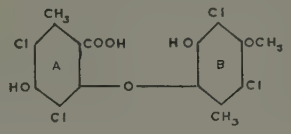
(*a*) Acidification of the sodium bicarbonate solution gave a brown gum which could not be obtained in a crystalline condition.

(*b*) The sodium hydroxide extract was acidified with dilute sulphuric acid and extracted with ether. Evaporation of the ether gave an oil which was repeatedly treated with hot petroleum ether (B.P. 60°–80°C.). On cooling, the solvent deposited crystals, which were recrystallised twice from aqueous methyl alcohol, giving colourless needles, M.P. 78°–79°C. The latter gave a violet coloration with ferric chloride, and the substance was identical with the synthetic 4·6–dichlor orsellinic acid methyl ester 5–monomethyl ether (VIII) described by Nolan and Murphy (*loc. cit.*).

Found :— C45·1, H3·9, OCH_3 23·9.

$C_8H_4O_2Cl_2(OCH_3)_2$ requires :—C45·3, H3·8, OCH_3 23·4.

2·4·3·′5′–tetrachlor—3·2′–dihydroxy—6–carboxy—4′–methoxy—5·6′–dimethyl diphenyl ether IX.



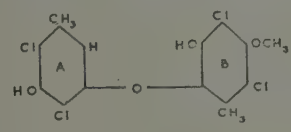
(IX)

Diploicin was hydrolysed by heating to gentle boiling with two per cent. aqueous sodium hydroxide. The liquor at first was pale yellow, afterwards slightly brownish. The heating was continued until practically all the solid had gone into solution (ca. fifteen minutes), then cooled, filtered, and acidified with dilute hydrochloric acid. The precipitate obtained was filtered, washed with water, and air dried. The product was crystallised several times from boiling benzene, and then dried in the air oven at 120°C. for several hours. The crystals thus obtained occurred both as colourless rhombohedra and as needles. M.P. 216°–218°C. (decomp.).

Found :— C43·93, H3·02.

$C_{16}H_{12}O_6Cl_4$ requires :— C43·44, H2·71.

2·4·3′·5′–tetrachlor—3·2′–dihydroxy—4′–methoxy—5·6′–dimethyl diphenyl ether X.



(X)

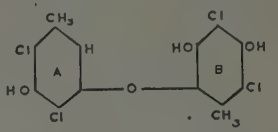
This compound was obtained by the elimination of carbon dioxide from the carboxylic acid IX above. Decarboxylation takes place very readily, and can be achieved in either of two ways.

Method I. The hydrolysis of diploicin described above was continued for a period of about one hour. When the solution thus obtained was saturated with carbon dioxide, most of the material was precipitated as a white solid, which did not contain a carboxyl group and had the di-tolyl ether structure X. Crystallisation from benzene gave colourless needles M.P. 186°C.

Method II. The carboxylic acid IX was heated above its melting point, when decomposition occurred with evolution of carbon dioxide. The resultant brown product was crystallised from dilute alcohol (norite) and afterwards from benzene, and was obtained as colourless needles M.P. 186°C., identical with the compound obtained by method I. The substance gives no colour with ferric chloride.

Found :— C45·45, H3·1, Cl35·4.
$C_{15}H_{12}O_4Cl_4$ requires :—C45·23, H3·02, Cl35·68.

2·4·3′·5′–tetrachlor—3·2′·4′–trihydroxy—5·6′–dimethyl diphenyl ether XI.



(XI)

This compound was produced by either of the following procedures.

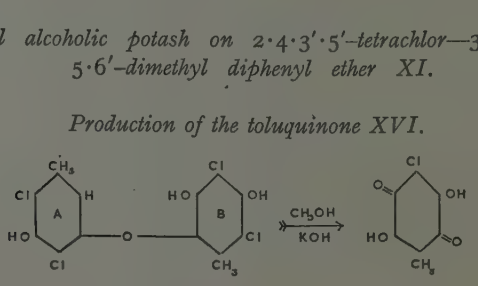
Method I. A mixture of the methoxy derivative X (9 g.), acetic acid (180 c.c.), constant boiling hydrobromic acid (150 c.c.) and red phosphorus (18 g.), was boiled under reflux for eight hours and was then cooled and filtered. The filtrate, on diluting largely with water, gave a small amount of cream precipitate. The residue of red phosphorus was extracted several times with boiling alcohol, filtered, and the alcoholic filtrate diluted with water, giving a considerable amount of white precipitate. The latter was crystallised from dilute alcohol, and furnished colourless, hexagonal crystals, M.P. 235°C.

Method II. Diploicin (1 g.) in acetic acid (20 c.c.) was heated with red phosphorus (2 g.) and constant boiling hydrobromic acid (16 c.c.) for eight hours, under reflux. After cooling the liquor was filtered, and the phosphorus washed with acetic acid. The whole of the filtrate was diluted with water and saturated with sodium bisulphite in order to decolorise it. A cream coloured precipitate was obtained. Further quantities of material were obtained by extraction of the phosphorus with hot alcohol. Crystallisation of the crude substance from hot dilute alcohol and boiling benzene gave colourless hexagons, M.P. 235°C. The mixed melting point of this substance with that obtained by method I was unchanged. Yield about 60 per cent.

Found :— C 44·53, H 2·96, Cl 36·35.
$C_{14}H_{10}O_4Cl_4$ requires :— C 43·7, H 2·6, Cl 37·0.

Action of methyl alcoholic potash on 2·4·3′·5′–tetrachlor—3·2′·4′–trihydroxy—5·6′–dimethyl diphenyl ether XI.

Production of the toluquinone XVI.



(XI) (XVI)

The compound XI (1·3 g.) was treated with five per cent. methyl alcoholic potash (30 c.c.), and heated under reflux at 60°C. for about three hours. Throughout this period, a slow stream of oxygen was bubbled through the solution. On standing overnight, the dark brown potassium salt of the quinone separated. This was filtered off, washed with a little methyl alcohol, dissolved in water, and acidified with dilute hydrochloric acid. The quinone was extracted with ether, the ether solution dried over anhydrous sodium sulphate, filtered, and evaporated to dryness, leaving a red crystalline residue. The latter was dissolved in the minimum volume of warm ethyl acetate, a large excess of chloroform added and the mixture allowed to stand. After a short time, garnet coloured hexagonal crystals of the quinone separated. The quinone sinters about 230°C., becomes black and melts about 264°C. (decomp.). The substance gives a violet colour with one per cent. aqueous sodium carbonate.

Found :— C 44·57, H 2·72, Cl 19..1.
$C_7H_5O_4Cl$ requires :— C 44.55, H 2.65, Cl 18.8.

Tetracetate of 4–chlor—2·3·5·6–tetrahydroxy toluene XVII.

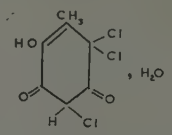
The toluquinone XVI was suspended in water, saturated with sulphur dioxide and the mixture allowed to stand for several days, the solution then having a very pale straw colour. Extraction of this solution with ether gave crude 4–chlor–2·3·5·6–tetrahydroxy toluene M.P. ca. 183°C., which tended to darken on exposure to the air. The air dried tetrahydroxy compound was dissolved in acetic anhydride to which a drop of concentrated sulphuric acid was added. After standing one hour, the mixture was diluted with water and extracted with ether. The ether solution was washed with water and dried over anhydrous sodium sulphate. The residue obtained on evaporation of the ether was crystallised from a mixture of benzene and ligroin and gave colourless prisms M.P. 219°C.

Found :— C 50·15, H 4·36, Cl 10·38.
$C_{15}H_{15}O_8Cl$ requires :— C 50·21, H 4·18, Cl 9·9.

2.4–dichlor—3·5·6–trihydroxy toluene XII.

To obtain this substance use was made of an observation of Heinrich, Meyer and Droschky (Ber. 37, 1904, p. 1427) that the action of hypochlorous acid on β–amino–orcin (which is 2–amino–orcin) gives rise to a product of formula $C_7H_7Cl_3O_4$. Heinrich did not attribute a structure to this substance, but the work of Zincke and his co-workers

(Zincke and Schurmann, Ann. 1918, 417, pp. 236–256) on the keto-chlorides suggested to us that it was a keto-chloride $C_7H_5Cl_3O_3$, H_2O to which the following formula, or one of similar type might be attributed :—



Heinrich's product was obtained by a modification of his method and on reduction with stannous chloride, it gave rise to a dichlor–trihydroxy toluene, for which the only possible formula appears to be XII above.

(*a*) *Chlorination of 2–amino–orcin.* 2–amino–orcin (4·7 g.) was added to a cooled mixture of acetic acid (18·8 c.c.) and concentrated hydrochloric acid (9·2 c.c.) and chlorine was passed through the mixture to saturation. The liquid was allowed to stand overnight and then poured into a dish and placed in a draught to remove excess chlorine. An equal volume of water was added and the solution cooled, when the yellow crystalline compound which was precipitated was filtered, washed with a little water and dried over sodium hydroxide in vacuo. (yield 2·2 g.). It was crystallised from benzene giving colourless crystals (0·6 g.) M.P. 92°–95°C. On addition of a little water to the benzene mother liquors, colourless needles of a hydrate crystallised out (0·65 g.). Softens 92°C., M.P. 96°–98°C.

Analysis of this hydrate gave the following results :—

Found :— C 31·0, H 2·75, Cl 38·75.

$C_7H_5Cl_3O_3$, $1\frac{1}{2}$ H_2O requires :— C 31·05, H 2·88, Cl 39·4.

(*b*) *Reduction of the keto-chloride.* The keto-chloride (0.8 g.) was dissolved in acetic acid (4 c.c.). To the solution stannous chloride (2·8 g.) in concentrated hydrochloric acid (10 c.c.) was added slowly, with cooling. A white crystalline mass separated. The mixture was allowed to stand overnight, in the dark, in a stoppered flask when the crystals were filtered, washed with 1 : 1 hydrochloric acid-water and air dried. Recrystallisation from benzene gave pale pinkish-brown needles M.P. 168°–172°C. The substance gives a port-wine colour with ferric chloride and a cerise coloration with one per cent. sodium carbonate.

Found :— C 40·3, H 2·92, Cl 33·5.

$C_7H_6O_3Cl_2$ requires :— C 40·2, H 2·87, Cl 34·0.

Action of methyl alcoholic potash on 2·4–dichlor–3·5·6–trihydroxy toluene XII.

Production of the toluquinone XVI.

2·4–dichlor–3·5·6–trihydroxy toluene (3 g.) was dissolved in five per cent. methyl alcoholic potash (60 c.c.). A transient green colour was produced which

rapidly changed to deep purple. The solution was heated under reflux at 40°–50°C. for two hours, while a slow stream of oxygen was bubbled through. On standing overnight, the dark brown precipitate which had separated was filtered, washed with a little methyl alcohol, dissolved in water and acidified with dilute hydrochloric acid. The liquor was extracted with ether, the ether dried over anhydrous sodium sulphate and evaporated, leaving a reddish residue. The residue on crystallisation from ethyl acetate-chloroform gave garnet coloured hexagonal crystals sintering about 230°C., which gave a violet coloration with one per cent. sodium carbonate.

Found :— C 44·24, H 3·2, Cl 18·7.

$C_7H_5O_4Cl$ requires :— C 44·55, H 2·65, Cl 18·8.

The identity of this substance with the toluquinone XVI, obtained by the action of methyl alcoholic potash on the di-tolyl ether XI, was shown in the following way. Reduction of the substance followed by acetylation gave the tetracetate of 4–chlor–2·3·5·6–tetrahydroxy toluene M.P. 219°C.

Found :— Cl 9·36, $C_{15}H_{15}O_8Cl$ requires :— Cl 9·9.

The mixed melting point of this tetracetate with XVII was unaltered.

2·6–*dichlor*—3·4·5–*trihydroxy toluene XIII.*

In the production of this compound, considerable difficulty was experienced in preparing the necessary starting substance, 3·4·5–trihydroxy toluene. Various methods were tried of which the following two proved the most satisfactory.

Method I. 3·4·5–trihydroxy toluene was prepared from atranol (2·6–dihydroxy–4–methyl benzaldehyde) by the Dakin reaction in accordance with the procedure described by St. Pfau (Helv. Chim. Acta, 9, p. 667) and was obtained as brown needles M.P. 125°–130°C. Yield 25 per cent.

Method II. The procedure described by Asahina (Ber. 69, 1936, p. 2328) was more convenient and gave somewhat better yields than method I. Galloyl chloride trimethyl ether was reduced by Rosenmund's method to gallic aldehyde trimethyl ether. The latter was reduced by hydrazine hydrate to 3·4·5–trimethoxy toluene which was then demethylated with acetic acid–hydrobromic acid and furnished brown needles of 3·4·5–trihydroxy toluene M.P. 119°C.

Chlorination of 3·4·5–*trihydroxy toluene.* 3·4·5–trihydroxy toluene (1 g.) prepared by either of the above methods, was dissolved in dry ether (15 c.c.) and sulphuryl chloride (2·1 g. in 5 c.c. ether) was added. A maroon colour developed and slight evolution of heat took place. After standing one hour, the solution was shaken with a little water. The ether solution was dried over anhydrous sodium sulphate, filtered, and evaporated in vacuo, leaving a pale brown residue. Crystallisation from benzene gave 0·6 g. pinkish white crystals, which did not melt sharply, but over a range of 170°–180°C.

Found :— Cl 33·7, $C_7H_6O_3Cl_2$ requires :— Cl 33·9.

With one per cent. sodium carbonate 2·6–dichlor–3·4·5–trihydroxy toluene gave a cerise coloration, turning brown on standing. With aqueous ferric chloride it gave a cobalt blue colour, fading to pale blue on standing.

Action of methyl alcoholic potash on 2·6–dichlor–3·4·5–trihydroxy toluene XIII.

2·6–dichlor–3·4..5–trihydroxy toluene was treated with five per cent. methyl alcoholic potash. The solution, initially pink, changed to blue and finally brown. The mixture was heated under the same conditions as described for the treatment of 2·4–dichlor–3·5·6–trihydroxy toluene above and the separated solid worked up in a similar manner. The only product obtained was a brown oil, which could not be induced to crystallise. No material of quinone type could be isolated from the reaction mixture.

2·3–dichlor–4·5·6–trihydroxy toluene XIV.

2·3·4–trihydroxy toluene was obtained by Clemmensen reduction of pyrogallol o-aldehyde (Dimroth and Zoeppritz, Ber. 35, 1902, p. 996) according to the method of Majima and Okazaki (Ber. 49, 1916, p. 1492) and crystallised from benzene in off white needles M.P. 140°C. Chlorination of this trihydroxy toluene was effected with sulphuryl chloride as described for the production of XIII. Chlorination did not appear to proceed so smoothly as in the latter case, but material was obtained which crystallised from benzene in faintly pink oval plates, M.P. 120°C. (decomp.). With one per cent. sodium carbonate it gave a yellow colour, turning brown rapidly. Alcoholic ferric chloride gave a pale green coloration, turning olive green rapidly.

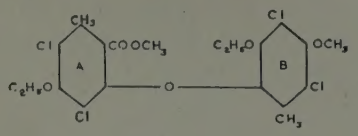
Found :— Cl 36·7, $C_7H_6O_3Cl_2$ requires :—Cl 33·9.

Although somewhat impure, the substance appeared to be the required dichloro derivative and was employed, without further purification in the following experiment.

Action of methyl alcoholic potash o 2·3–dichlor–4·5·6–trihydroxy toluene XIV.

2·3–dichlor–4·5·6–trihydroxy toluene was warmed with five per cent. methyl alcoholic potash under conditions similar to those described above for XII and XIII. Only brown oily material, which could not be induced to crystallise, was isolated from the reaction product. There was no indication of the formation of a quinone.

2·4·3′·5′–tetrachlor—3·2′–diethoxy—4′–methoxy—6–carbomethoxy—5·6′–dimethyl diphenyl ether.



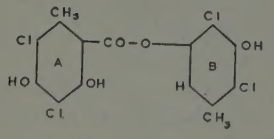
Treatment of the substance V with diazo-ethane and crystallisation of the product from methyl alcohol gave the above compound as colourless crystals M.P. 94°–95°C.

Found :— C 48·63, H 4·1, Cl 27·9.

$C_{15}H_6O_2Cl_4(OCH_3)_2(OC_2H_5)_2$ requires :— C 49·2, H 4·3, Cl 27·7.

This compound cannot be identical with the tetrachloro derivative obtained from gangaleoidin and mentioned in the introductory part, as the latter melts at 76°–77°C.

(*2·4–dichlor—3–hydroxy—5–methyl*) *phenylester of 4..6–dichlor—orsellinic acid XVIII.*



Diploicin (5 grms.) was dissolved in the minimum volume of boiling dry benzene anhydrous aluminium chloride (7 grms.) was added and the mixture refluxed on the steam bath for six hours. After standing overnight, the solvent was decanted and the residue decomposed with ice and dilute hydrochloric acid. It was then extracted with ether and the ether solution extracted several times with dilute sodium bicarbonate. Acidification of the sodium bicarbonate solution gave a white precipitate, which was washed with water, air dried and crystallised from benzene, in which it was sparingly soluble. The pure substance crystallises in pale yellow prisms M.P. 206°C. Yield 2·8 grms. The compound gives a faint reddish brown colour with ferric chloride and a yellow colour with bleaching powder solution. It dissolves in dilute sodium carbonate to a faintly yellow solution which does not give a violet colour on standing.

Found :— C 42·09, H 2·52, Cl 32·6.

$C_{15}H_{10}O_6Cl_4$ requires :— C 42·05, H 2·33, Cl 33·1.

Diploicin was recovered unchanged from the material insoluble in dilute sodium bicarbonate.

Acetylation of the compound with acetic anhydride and a trace of sulphuric acid gave a triacetate which crystallised from benzene and ligroin in colourless prisms M.P. 175°–176°C.

Found :— C 45·99, H 2·89, Cl 25·8.

$C_{15}H_7O_6Cl_4(CH_3CO)_3$ requires :— C 45·49, H 2·88, Cl 25·7.

Methylation of the compound with diazo-methane gave a trimethyl ether which crystallised from methyl alcohol in colourless prisms M.P. 184°C.

Found :— C 47·36, H 2·92, Cl 31·3.

$C_{15}H_7O_2Cl_4(OCH_3)_3$ requires :— C 47·57, H 3·5, Cl 31·2.

Action of methyl alcoholic potash on the compound XVIII.

Compound XVIII (1·3 grms.) in five per cent. methyl alcoholic potash (40 c.c.) was heated at 60°–70°C. for four hours while a slow stream of oxygen was bubbled through the solution. After standing overnight, the mother liquor was filtered from precipitated dark brown solid. The latter was dissolved in a little water, acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the ether gave a reddish brown residue which crystallised from ethyl acetate-chloroform in garnet coloured hexagons (0·1 grm.), which sintered at 230°C. The identity of this compound with the toluquinone obtained from the ditolyl ether XI and from 2·4-dichlor–trihydroxy toluene XII was shown in the following manner. The substance was reduced with aqueous sulphur dioxide and the resultant product acetylated. The tetracetate thus obtained melted at 219°C. and was identical (mixed melt) with the compound XVII previously described.

The mother liquor, above, from the dark brown solid was saturated with carbon dioxide, diluted with water and extracted with ether. On evaporation of the ether and crystallisation of the residue from aqueous alcohol, colourless needles were obtained M.P. 120°–121C°., giving a violet coloration with ferric chloride. Analysis showed this substance to be the methyl ester of 4·6–dichlor–orsellinic acid VI, containing one molecule of water of crystallisation. A mixed melting point with the methyl ester of 4·6–dichlor–orsellinic acid (M.P. 115°–117°C.) synthesised by Nolan and Murphy (*loc. cit.*) melted at 115°–117°C.

Found :— C 39·48, H 4·01, Cl 26·3.

$C_9H_8O_4Cl_2$, H_2O requires :— C 40·14, H 3·71, Cl 26·4.

That this substance was actually the methyl ester of 4·6–dichlor–orsellinic acid VI was shown in the following way. The compound was acetylated and gave a diacetate which crystallised from aqueous alcohol in colourless prisms M.P. 93°C. and gave no colour with ferric chloride.

Found :— C 46·66, H 3·44, Cl 21·6.

$C_9H_6O_4Cl_2(CH_3CO)_2$ requires :— C 46·56, H 3·58, Cl 21·2.

The mixed melting point of this diacetate with the diacetate of 4·6–dichlor–orsellinic acid methyl ester, prepared in the manner described below, was unaltered.

A specimen of o-orsellinic acid methyl ester from lecanoric acid was chlorinated with sulphuryl chloride to give crude 4·6–dichlor–orsellinic acid methyl ester (M.P. ca 115°C.). The latter was acetylated and gave on crystallisation from aqueous alcohol a diacetate M.P. 93°C.